

410 Rec'd PCT/PTO 0 2 JUN 2000

FORM PTO-1590 (REV. 1-98)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER 427.035	
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371					
INTERNATIONAL APPLICATION NO. PCT/FR98/02576		INTERNATIONAL FILING DATE December 1, 1998		PRIORITY DATE CLAIMED December 3, 1997	
TITLE OF INVENTION USE OF EXTRACTS OF GINKGO BILOBA FOR PREPARING A MEDICAMENT					
APPLICANT(S) FOR DO/EO/US Katy DRIEU					
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:					
1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. 2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. 3. <input type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1). 4. <input type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date. 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) a. <input checked="" type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> has been transmitted by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input checked="" type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)). 7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> have been transmitted by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)). 9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). UNEXECUTED 10. <input type="checkbox"/> A translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).					
Items 11. to 16. below concern document(s) or information included:					
11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 13. <input checked="" type="checkbox"/> A FIRST preliminary amendment. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. 14. <input type="checkbox"/> A substitute specification. 15. <input type="checkbox"/> A change of power of attorney and/or address letter. 16. <input checked="" type="checkbox"/> Other items or information: PCT/IB/332; French International Preliminary Examination Report					



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Our Ref.: 427.035

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: :  
Katy DRIEU : PCT Date: December 1, 1998  
PCT/FR98/02576 :  
Serial No.: :  
Filed: Concurrently Herewith :  
For: USE OF EXTRACTS OF GINKGO :  
BILOBA FOR PREPARING A :  
MEDICAMENT :  
600 Third Avenue  
New York, NY 10016

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Please amend this application as follows:

IN THE SPECIFICATION:

Page 1, before line 1, insert

--This application is a 371 of PCT/FR98/02576 filed  
December 1, 1998.--

IN THE CLAIMS:

Please cancel claims 1 and 9 and add the following claims.

--11. A method of easing withdrawal symptoms of substance  
dependency or addiction in a human being comprising administering

to a human being in need thereof a Ginkgo biloba extract in an amount sufficient to ease withdrawal symptoms.

12. The method of claim 11 wherein the substance is selected from the group consisting of alcohol, tobacco, amphetamines and drugs inducing toxicomania.

13. The method of claim 11 wherein the extract is selected from the group consisting of ginkgolide, a pharmaceutical salt thereof or a glycosylated, alkoxyated or acetylated ginkgolide.--

Claims 2 to 4, line 1 of each, cancel "Use according to claim 1" and insert --The method of claim 11--.

Claim 5, line 1, cancel "Use according to" and insert --The method of--.

Claim 6, cancel line 1 and insert --The method of claim 11 wherein the extract contains a compound of the formula--.

Claim 7, line 1, cancel "Use according to" and insert --The method of--.


Claim 8, cancel line 1 and insert --The method of claim 6 wherein--.

Claim 10, line 1, cancel "Use according to claim 9" and insert  
--The method of claim 13--.

REMARKS

The amendment is filed to refer to the PCT application and to  
conform the claims to the American practice.

Respectfully submitted,  
BIERMAN, MUSERLIAN AND LUCAS

  
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CAM:sd

Enclosure: Return Receipt Postcard

**Use of extracts of Ginkgo biloba for preparing a medicament**

The invention relates to the use of extracts of Ginkgo biloba for preparing a medicament intended to ease the withdrawal of individuals who are dependent on the consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, amphetamines, tobacco, drugs inducing toxicomania.

- 5 It is already known that extracts of Ginkgo biloba have an activity in the cardiovascular field (in particular the reduction of platelet adhesion), in the central nervous field (in particular a neuroprotective activity) or in the neurosensory system (in particular retinal protection); cf. for example DeFeudis et al., Ginkgo Biloba Extract (EGb 761®), Pharmaceutical Activities and Clinical Applications (Elsevier, Paris, 1991). Their  
10 preparation has been the subject of a certain number of patents, of which there can be mentioned the European Patents EP 431 535 and EP 431 536, and the American Patent US 5,389,370.

- Now the Applicant has just found that certain extracts of Ginkgo biloba also have useful new pharmacological properties, namely easing the withdrawal of subjects addicted to  
15 alcohol or drugs, and more generally of subjects dependent on a substance engendering dependency and/or addiction. The Applicant observed that the administration of these extracts resulted in an attenuation of the withdrawal symptoms.

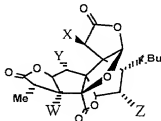
- A subject of the invention is therefore the use of these extracts for preparing a medicament intended to ease the withdrawal of individuals dependent on the  
20 consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, amphetamines, tobacco, drugs inducing toxicomania.

By drugs inducing toxicomania is understood in particular morphine and its derivatives, opium and opiates, cocaine, crack, and more generally all substances, including any medicamentous substances, on which a subject can become dependent.

- 25 By extract of Ginkgo biloba is understood at least one of the individual compounds which can be obtained by extraction from the *Ginkgo biloba* L tree, and in particular a

flavonoid compound or a terpene such as a ginkgolide or a bilobalide, or also a mixture of the latter. Preferably, the extract used will be such that it contains an effective quantity of ginkgolides. For the uses according to the invention, an extract of type EGb 761 or CP 401 can for example be chosen.

- 5 By ginkgolide is understood all the natural ginkgolides obtained from the *Ginkgo biloba* tree, as well as synthetic ginkgolides and their derivatives (resulting for example from an acetylation or alkoxylation reaction) and pharmaceutically active salts. The ginkgolides used can for example be ginkgolide A, ginkgolide B, ginkgolide C, ginkgolide J or ginkgolide M (structures given in the diagram below; these compounds
- 10 can be isolated from extracts of *Ginkgo biloba* leaves - see *GINKGOLIDES, Chemistry, Biology, Pharmacology and Clinical Perspectives*, published by P. Braquet, J.R. Prous Science Publishers, in particular Volumes 1 (1988) and 2 (1989)). Glycosylated derivatives of ginkgolides or alkoxyated or acetylated derivatives of ginkgolides can also be used. By alkoxyated derivative of ginkgolide is understood a ginkgolide
- 15 derivative comprising at least one linear or branched alkoxy group, instead of a hydroxy group (these compounds are described in French Patent Application No. FR 88.14392). Similarly, by acetylated derivative of ginkgolide is understood a derivative of ginkgolide comprising at least one acetate group instead of a hydroxy group.



20

Ginkgolide	W	X	Y	Z
A	OH	OH	H	H
B	OH	OH	OH	H
C	OH	OH	OH	OH
J	OH	OH	H	OH
M	H	OH	OH	OH

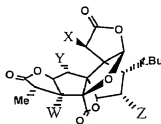
Structure of ginkgolides A, B, C, J and M

By extract of type EGb 761 is understood an extract of a composition substantially identical to that of the standardized extract EGb 761 as defined in particular in the

- following article: K. Drieu, La presse médicale, 31, 25 September 1986, supplement devoted to the extract of Ginkgo biloba (EGb 761), 1455-1457; or in the European Patents EP 431 535 and EP 431 536; by extract of type EGb 761 is therefore understood in particular extracts of Ginkgo biloba comprising 20 to 30 % of flavoneglycosides, 2.5 to 4.5 % of ginkgolides A, B, C and J, 2 to 4 % of bilobalide, less than 10 % of proanthocyanidines and less than 10 ppm, and preferably less than 5 ppm, of compounds of alkylphenol type, and in particular extracts of Ginkgo biloba comprising approximately 24 % of flavoneglycosides, 3.1 % of ginkgolides A, B, C and J, 2.9 % of bilobalide, 6.5 % of proanthocyanidines and less than 1 ppm of compounds of alkylphenol type. By extract of type CP 401 is understood extracts such as those which are presented in the Patent US 5,389,370, in particular extracts of Ginkgo biloba containing 5.5 to 8 % of ginkgolides A, B, C and J, 40 to 60 % of flavoneglycosides and 5 to 7 % of bilobalide, and quite particularly extracts containing approximately 7 % of ginkgolides A, B, C and J, 50 % of flavoneglycosides and 6 % of bilobalide.
- According to another aspect of the invention, the extract of Ginkgo biloba used will comprise more than 5 % of ginkgolides, and more preferably more than 50 % of ginkgolides.

- The invention also relates to the use of a ginkgolide or one of its derivatives or pharmaceutically active salts for preparing a medicament intended to ease the withdrawal of individuals dependent on the consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, amphetamines, tobacco, drugs inducing toxicomania. Preferably, the ginkgolide used for this aspect of the invention will be ginkgolide A or ginkgolide B.

The invention also relates to the use of a compound of general formula (I)



(I)

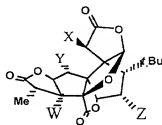
in which W, X, Y and Z independently represent the H, OH, linear or branched alkoxy or O-G<sub>S</sub>, G<sub>S</sub>-OH radicals representing a mono- or disaccharide, or one of their derivatives or analogues,



it being understood that at least one of W, X, Y or Z represents an O-G<sub>S</sub> radical,

for preparing a medicament intended to ease the withdrawal of individuals dependent on the consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, tobacco, amphetamines, drugs inducing toxicomania.

- 5 The invention preferably relates to the use of a compound of general formula (I)



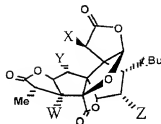
(I)

in which X represents an OH or O-G<sub>S</sub> radical, G<sub>S</sub>-OH representing a mono- or disaccharide, or one of their derivatives or analogues, and:

- either W represents an OH or O-G<sub>S</sub> radical, Y represents H and Z represents H;
- 10 - or W represents an OH or O-G<sub>S</sub> radical, Y represents an OH or O-G<sub>S</sub> radical and Z represents H;
- or W represents an OH or O-G<sub>S</sub> radical, Y represents an OH or O-G<sub>S</sub> radical and Z represents an OH or O-G<sub>S</sub> radical;
- or W represents an OH or O-G<sub>S</sub> radical, Y represents H and Z represents an OH or O-G<sub>S</sub> radical;
- 15 - or W represents H, Y represents an OH or O-G<sub>S</sub> radical and Z represents an OH or O-G<sub>S</sub> radical;
- or W represents an OH or O-G<sub>S</sub> radical, Y represents a linear or branched alkoxy radical and Z represents H;
- 20 it being understood that at least one of W, X, Y or Z represents an O-G<sub>S</sub> radical,

for preparing a medicament intended to ease the withdrawal of individuals dependent on the consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, tobacco, amphetamines, drugs inducing toxicomania.

The invention relates quite particularly to the use of a compound of general formula (I)



(I)

in which X represents an OH or O-G<sub>S</sub> radical, G<sub>S</sub>-OH representing a mono- or disaccharide, or one of their derivatives or analogues, and:

- either W represents an OH or O-G<sub>S</sub> radical, Y represents H and Z represents H;

- 5 - or W represents an OH or O-G<sub>S</sub> radical, Y represents an OH or O-G<sub>S</sub> radical and Z represents H;

- or W represents an OH or O-G<sub>S</sub> radical, Y represents a linear or branched alkoxy radical and Z represents H;

it being understood that at least one of W, X, Y or Z represents an O-G<sub>S</sub> radical,

- 10 for preparing a medicament intended to ease the withdrawal of individuals dependent on the consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, tobacco, amphetamines, drugs inducing toxicomania.

- By linear or branched alkoxy radical is understood in the present description an alkoxy radical the linear or branched carbon containing chain of which contains 1 to 6 carbon  
15 atoms. By derivative or analogue of mono- or disaccharides is understood compounds such as N-acetylglucosamine, N-acetylalosamine, galactosamine, mannoseamine, N-tosylhydrazine, etc.

- Preferably, O-G<sub>S</sub> will be chosen such that G<sub>S</sub>-OH belongs to the group comprising abequeose, rhamnose, arabinose, ribose, xylose, 2-deoxy-ribose, glucose, galactose,  
20 mannose, 2-deoxyglucose, fructose, fucose, N-acetylglucosamine, N-acetylalosamine, galactosamine, mannamine, saccharose, lactose, maltose, cellobiose and trehalose. Even more preferentially, O-G<sub>S</sub> will be chosen such that G<sub>S</sub>-OH belongs to the group comprising glucose and lactose.

- The invention therefore also relates to the use of glycosylated derivatives of  
25 ginkgolides, more particularly those of ginkgolides A and B, the glycosyl groups suitable for the invention having been described previously.

The different processes for obtaining glycosylated derivatives of ginkgolides or alkoxyated ginkgolides (i.e. those resulting from a glycosylation reaction carried out on at least one of the OH groups of ginkgolides or their alkoxyated derivatives) are described in the following publication: Weber, M. and Vasella, A., *Helv. Chim. Acta*, 80  
5 (1997), 2352-2367.

The pharmaceutical compositions comprising a compound of the invention can be in the form of solids, for example powders, granules, tablets, gelatin capsules, liposomes or suppositories. Appropriate solid supports can be, for example, calcium phosphate, magnesium stearate, talc, sugars, lactose, dextrin, starch, gelatin, cellulose, methyl  
10 cellulose, sodium carboxymethyl cellulose, polyvinylpyrrolidone and wax.

The pharmaceutical compositions containing a compound of the invention can also be presented in liquid form, for example, solutions, emulsions, suspensions or syrups. Appropriate liquid supports can be, for example, water, organic solvents such as glycerol or glycols, as well as their mixtures, in varying proportions, in water.

15 The administration of a medicament according to the invention can be carried out by topical, oral, parenteral route, by injection (intramuscular, sub-cutaneous, intravenous, etc.), etc.

The administration dose envisaged for a medicament according to the invention is comprised between 0.1 mg and 10 g according to the type of substance on which the  
20 subject to be treated is dependent.

Unless they are defined differently, all the technical and scientific terms used here have the same meaning as that usually understood by an ordinary specialist in the field to which this invention belongs. Similarly, all publications, patent applications, all patents and all other references mentioned here are incorporated by way of reference.

**Pharmacological study of the products of the invention:**

**1. Study of the effects of extracts of Ginkgo biloba on alcohol dependency:**

Two studies were carried out: one relates to the effects of EGb 761, the other to the effects of another extract of Ginkgo biloba, CP 401, which does not contain bilobalide but twice as much ginkgolides as EGb 761 (6 %).

- 1) Rats are treated for 15 days with alcohol (they are administered 10 % ethanol in their drinking water for the first week and then 12.5 % ethanol). They are given 50 or 100 mg/kg of EGb 761 per day by oral route (gavage) for the 5 days before the absorption of alcohol is stopped (from the 11th day) and the 3 days after it is stopped.
- 10 The behavioural symptoms were evaluated for 3 days after the absorption of alcohol is stopped in three groups of rats (n=6): the control group having received only alcohol, one group having received alcohol and treatment with 50 mg/kg of EGb 761 and another group having received alcohol and treatment with 100 mg/kg of EGb 761, the treatments with EGb 761 having been administered under the conditions described
- 15 above. The results of these tests are shown in table (I) which can be found in appendix I.

In the animals which received EGb 761, it can be observed that the withdrawal symptoms (7 criteria) are reduced in a dose-dependent manner and that the animals also have reduced motor hyperactivity.

- 20 2) Rats are treated for 15 days with alcohol (they are given 10 % ethanol in their drinking water for the first week and then 12.5 % ethanol). They are administered 50 mg/kg of CP 401 extract per day by oral route (gavage) for the 5 days before the absorption of alcohol is stopped (from the 11th day) and the 3 days after it is stopped.
- The behavioural symptoms were evaluated for the 3 days after the absorption of alcohol
- 25 was stopped in three groups of rats (n=6): the control group only having received alcohol and the other group having received alcohol and treatment with 50 mg/kg of CP 401 extract administered under the conditions described above. The results of these tests are shown in table (II) which can be found in appendix I.

- It is observed that the animals which received the CP 401 extract show a reduction in
- 30 the symptoms linked with withdrawal compared with the intoxicated control animals.

## 2. Study of the effects of Ginkgo biloba extracts on sensitization to amphetamine:

An injection of amphetamine (0.5 mg/kg IP) provokes motor hyperactivity in the rat (measured by actimetry). Administration eight times, every other day, of the same dose of amphetamine results in a progressive increase in locomotive activity: this phenomenon is called "sensitization".

For 8 days before the administration of amphetamine and throughout this administration, rats (n=8) subjected to the administration of amphetamine as described above were subjected to treatment by oral route with a dose of EGb 761 of 100 mg/kg per day or of a dose of 5 mg/kg per day of ginkgolide A .

Actimetry measurements were carried out for 1 hour after the administration of the amphetamine on the 9th (first day on which amphetamine was administered), 13th, 17th, 21st and 25th day. The results of these tests are shown in A which can be found in appendix II.

It is observed that behavioural sensitization to amphetamine is reduced in the animals which received 5 mg/kg per day of ginkgolide A. An enhanced and quite significant effect is observed with EGb 761 at 100 mg/kg per day.

## 3. Study of the effects of Ginkgo biloba extract EGb 761 on morphine withdrawal syndrome:

Rats are treated every 8 hours (3 times per day) for 10 days with a dose of morphine by sub-cutaneous route resulting in motor hyperactivity (measured by actimetry). On the 11th day, they are administered naloxone (3 mg/kg IP) and the withdrawal signs are observed for 60 minutes: a series of behavioural signs is quantified, a series measured (hypothermia, weight loss) or a series graded (scale with 4 levels).

Two groups of 8 rats are treated with EGb 761 (50 or 100 mg/kg per day) for 4 days before the administration of naloxone and 2 hours before it. A group of intoxicated control rats only receives injections of morphine before the naloxone and an absolute control group only receives naloxone.

Statistical analysis of the batches is carried out using the following tests: parametric Anova, Barlett's test to check the homogeneity of variances and Dunnett's test for multiple comparisons.

The results quantified by counting for the different behavioural parameters analyzed are shown in table (III) which can be found in appendix III.

# APPENDIX I

Treatment (mg/kg)	TRE	SNO	CHA	TWI	MOT	ESC	JUM
none	7	17	15	12	11	6	5
EGb 761 (50)	5	9	8	6	6	3	2
EGb 761 (100)	0	5	4	2	3	0	1

*Table I - Influence of treatment with substance EGb 761 on the number of observations of each symptom of abstinence at 24 hours after withdrawal*

Treatment (mg/kg)	TRE	SNO	CHA	TWI	MOT	ESC	JUM
none	6	19	12	15	9	6	6
CP 401 (50)	4	11	6	7	5	4	3

*Table II - Influence of treatment with substance CP 401 on the number of observations of each symptom of abstinence at 24 hours after withdrawal*

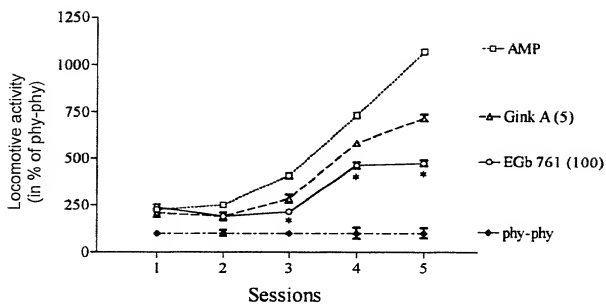
## Legend common to Tables I and II

TRE:	trembling in body
SNO:	snorting
CHA:	chattering of teeth
TWI:	twitching of ears
MOT:	motor activity
ESC:	attempted escapes
JUM:	jumps

The symptoms are graded from 0 to 3 according to their intensity (0 = slight; 3 = very pronounced).

## APPENDIX II

### Effect of substances EGb 761 and Ginkgolide A on sensitization to amphetamine



(\*) significantly different from amphetamine group ( $p < 0.05$ )



### APPENDIX III

Symptoms	Group 1	Group 2	Group 3
<b>Jumps</b>	0.0 ± 0.0	1.00 ± 0.33	0.50 ± 0.19
<b>Stiffening</b>	9.88 ± 1.03	1.13 ± 0.40	5.63 ± 1.00
<b>Snorting</b>	0.25 ± 0.16	2.75 ± 0.70	0.88 ± 0.29
<b>Jerking of head</b>	0.0 ± 0.0	5.50 ± 1.13	2.43 ± 0.48
<b>Yawning</b>	0.75 ± 0.41	2.00 ± 0.78	0.88 ± 0.40
<b>Chattering or grinding of teeth</b>	0.0 ± 0.0	4.75 ± 0.86	1.75 ± 0.45
<b>Burying</b>	0.25 ± 0.16	1.38 ± 0.46	0.25 ± 0.16
<b>Excessive scratching</b>	0.0 ± 0.0	1.13 ± 0.48	0.38 ± 0.26
<b>Grooming</b>	6.00 ± 1.39	1.38 ± 0.53	4.25 ± 1.31

*Table III - Influence of treatment with substance EGb 761 on the number of observations of each of the symptoms of abstinence during morphine withdrawal*

Legend:

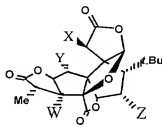
Group 1: control;

Group 2: group treated only with morphine (3 times 10 mg/kg/day);

Group 3: group treated with morphine and with EGb 761 at a dose of 100 mg/kg.

### Claims

1. Use of a Ginkgo biloba extract for preparing a medicament intended to ease the withdrawal of individuals dependent on the consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, amphetamines, tobacco, drugs inducing toxicomania.
2. Use according to claim 1, characterized in that the Ginkgo biloba extract is an extract of type EGb 761.
3. Use according to claim 1, characterized in that the Ginkgo biloba extract is an extract of type CP 401.
4. Use according to claim 1, characterized in that the Ginkgo biloba extract contains at least 5 % of ginkgolides.
5. Use according to claim 4, characterized in that the Ginkgo biloba extract contains at least 50 % of ginkgolides.
6. Use of a compound of general formula (I)



(I)

in which W, X, Y and Z independently represent the H, OH, linear or branched alkoxy or O-G<sub>S</sub> radicals, G<sub>S</sub>-OH representing a mono- or a disaccharide, or one of their derivatives or analogues,

it being understood that at least one of W, X, Y or Z represents an O-G<sub>S</sub> radical,

- for preparing a medicament intended to ease the withdrawal of individuals dependent on the consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, amphetamines, tobacco, drugs inducing toxicomania.

7. Use according to claim 6, characterized in that:

- either W represents an OH or O-G<sub>S</sub> radical, Y represents H and Z represents H;

- or W represents an OH or O-G<sub>S</sub> radical, Y represents an OH or O-G<sub>S</sub> radical and Z represents H;

5    - or W represents an OH or O-G<sub>S</sub> radical, Y represents an OH or O-G<sub>S</sub> radical and Z represents an OH or O-G<sub>S</sub> radical;

- or W represents an OH or O-G<sub>S</sub> radical, Y represents H and Z represents an OH or O-G<sub>S</sub> radical;

10    - or W represents H, Y represents an OH or O-G<sub>S</sub> radical and Z represents an OH or O-G<sub>S</sub> radical;

- or W represents an OH or O-G<sub>S</sub> radical, Y represents a linear or branched alkoxy radical and Z represents H;

it being understood that at least one of W, X, Y or Z represents an O-G<sub>S</sub> radical

8. Use according to claim 6 or 7, characterized in that:

15    - either W represents an OH or O-G<sub>S</sub> radical, Y represents H and Z represents H;

- or W represents an OH or O-G<sub>S</sub> radical, Y represents an OH or O-G<sub>S</sub> radical and Z represents H;

- or W represents an OH or O-G<sub>S</sub> radical, Y represents a linear or branched alkoxy radical and Z represents H;

20    it being understood that at least one of W, X, Y or Z represents an O-G<sub>S</sub> radical

9. Use of a ginkgolide or one of its glycosylated, alkoxylated or acetylated derivatives, or of a pharmaceutically active salt of the latter for preparing a medicament intended to ease the withdrawal of individuals dependent on the consumption of a substance engendering habituation and/or addiction, such as in particular alcohol, amphetamines, tobacco, drugs inducing toxicomania.

25    10. Use according to claim 9, characterized in that the ginkgolide is ginkgolide A or ginkgolide B.

ABSTRACT

The invention relates to the use of Ginkgo biloba extracts for preparing a medicament intended to ease the withdrawal of individuals dependent on the consumption of a substance engendering dependency and/or addiction, such as in particular alcohol, amphetamines, tobacco, drugs inducing toxicomania.

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UTILITY OR DESIGN  
PATENT APPLICATION☒ Declaration OR ☐ Declaration  
Submitted Submitted after  
with Initial Filing Initial Filing

Attorney Docket Number	427.035
First Named Inventor	Katy DRIEU
COMPLETE IF KNOWN	
Application Number	PCT/FR98/02576
Filing Date	December 1, 1998
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

USE OF EXTRACTS OF GINKGO BILOBA FOR PREPARING A MEDICAMENT

(Title of the invention)

the specification of which

☐ is attached hereto

OR

☒ was filed on (MM/DD/YYYY)

12/01/98

as United States Application Number or PCT International

Application Number

PCT/FR98/02576

and was amended on (MM/DD/YYYY)

(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, §1.56

I hereby claim foreign priority benefits under Title 35, United States Code §119 (a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §305 (a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?	
				YES	NO
97/15230*	France	12/03/97	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
PCT/FR98/02576 PCT		12/01/98			

☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto:

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	<input type="checkbox"/> Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

Person type a plus sign (+) inside this box → ☐Approved for use through 9/30/98. OMB 0651-0022  
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## DECLARATION

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Name	Registration Number	Name	Registration Number
Bierman, Muserlian and Lucas	18,818		
Jordan B. Bierman	18,629		
Charles A. Muserlian	19,683		
Donald C. Lucas	31,275		

☐ Additional registered practitioner(s) named on a supplemental sheet attached hereto.

Direct all correspondence to:

Name	Charles A. Muserlian		
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Address	600 Third Avenue		
City	New York	State	NY
Country	U.S.A.	Telephone	(212) 661-8000
		Fax	(212) 661-8002

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: ☐ A petition has been filed for this unsigned inventor

Given Name	Katy	Middle Initial		Family Name	DRIEU	Suffix e.g. Jr.	
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Inventor's Signature		Date	
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Residence: City	Paris	State		Country	France FRX	Citizenship	France
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Post Office Address			
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City	Paris	State		Zip	F-75015	Country	France
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☐ Additional inventors are being named on supplemental sheet(s) attached hereto